

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Patent No. : 6,573,099 Serial No.: 09/100,812  
Issue Date : June 3, 2003 Filed: June 19, 1998  
Inventors : Michael Wayne Graham, Peter Michael Waterhouse,  
and Robert Norman Rice  
Patent Owner : Commonwealth Scientific and Industrial Research  
Organisation  
For : GENETIC CONSTRUCTS FOR DELAYING OR REPRESSING  
THE EXPRESSION OF A TARGET GENE

30 Rockefeller Plaza,  
20th Floor  
New York, New York 10112

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**STATEMENT BY MICHAEL WAYNE GRAHAM UNDER 37 C.F.R. §1.324(b) (2)**

I, Michael Wayne Graham, hereby state as follows:

1. I understand that Peter Michael Waterhouse is being added as an inventor of the subject matter claimed in the above-identified patent, the claims of which are attached hereto as **Exhibit 1**, along with Robert Norman Rice and myself.
2. I have no disagreement in regard to the requested change.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject patent.

  
Michael Wayne Graham

Date:

22 March 2011

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 2 of 13 of Amendment

**Amendments to the Claims:**

Please amend the claims of the subject patent pursuant to 37 C.F.R. § 1.530(d)(2):

1-3. (Canceled)

4. (Amended) An isolated [genetic] double-stranded DNA construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said [genetic] double-stranded DNA construct, wherein said [genetic] double-stranded DNA construct comprises at least two identical copies of a structural gene sequence and each identical copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to [at least] a region of said target gene, wherein at least one identical copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other identical copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence.

Patent Owners : Michael Wayne Graham and Robert Norman Rice

**Reexamination**

Control Nos. : 90/007,247 and 90/008,096

Patent No. : 6,573,099 B2

Page 3 of 13 of Amendment

5. (Amended) An isolated [genetic] double-stranded DNA construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said [genetic] double-stranded DNA construct, wherein said [genetic] double-stranded DNA construct comprises at least two identical copies of a structural gene sequence, wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to [at least] a region of said target gene, and wherein said at least two identical copies of said structural gene sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one identical copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence, wherein at least one other identical copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence, and wherein said at least one identical copy of said structural gene sequence that is placed in the sense orientation relative to said promoter and said at least one identical copy of said structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
**Control Nos. : 90/007,247 and 90/008,096**  
Patent No. : 6,573,099 B2  
Page 4 of 13 of Amendment

6. (Five Times Amended) An animal cell comprising the [genetic] double-stranded DNA construct of [any one of] claim[s 1-2 or 3-] 5.
7. (Four Times Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising transfecting said animal cell with a [genetic] double-stranded DNA construct, wherein said [genetic] double-stranded DNA construct comprises at least two identical copies of a structural gene sequence, wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to [at least] a region of said target gene, and wherein said at least two identical copies of said structural gene sequence are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one identical copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence and wherein at least one other identical copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence, wherein said identical copy of said structural gene sequence that is placed in the sense orientation relative to said promoter and said identical copy of said structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.
- 8-9. (Canceled)

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 5 of 13 of Amendment

10. (Three Times Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising expressing in said animal cell a [genetic] double-stranded DNA construct, wherein said [genetic] double-stranded DNA construct comprises at least two identical copies of a structural gene sequence, wherein each identical copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to [at least] a region of said target gene, wherein at least one identical copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other identical copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence.
11. (Five Times Amended) The isolated [genetic] double-stranded DNA construct according to [any one of] claim[s] 1, 2 or 3-] 5, wherein said region of the target gene is [20 to] 30 nucleotides long.
12. (Four Times Amended) The method according to [any one of] claim[s] 7[-9 or 10], wherein said region of the target gene is [20 to] 30 nucleotides long.

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 6 of 13 of Amendment

13. (Five Times Amended) The isolated [genetic] double-stranded DNA construct according to [any one of] claim[s] 1, 2 or 3-] 5, comprising two identical copies of said structural gene sequence.
14. (Five Times Amended) The isolated [genetic] double-stranded DNA construct according to [any one of] claim[s] 1, 2 or 3-] 5, wherein said region of the target gene is [at least] more than 30 nucleotides long.
15. (Five Times Amended) The isolated [genetic] double-stranded DNA construct according to [any one of] claim[s] 1, 2 or 3-] 5, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.
16. (Five Times Amended) The method according to [any one of] claim[s] 7[-9 or 10], wherein said [genetic] double-stranded DNA construct comprises two identical copies of said structural gene sequence.
17. (Four Times Amended) The method according to [any one of] claim[s] 7[-9 or 10], wherein said region of the target gene is [at least] more than 30 nucleotides long.
18. (Four Times Amended) The method according to [any one of] claim[s] 7[-9 or 10], wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.
19. (Amended) An animal cell comprising the [genetic] double-stranded DNA construct according to claim 11.

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 7 of 13 of Amendment

20. (Amended) An animal cell comprising the [genetic] double-stranded DNA construct according to claim 13.
21. (Amended) An animal cell comprising the [genetic] double-stranded DNA construct according to claim 14.
22. (Amended) An animal cell comprising the [genetic] double-stranded DNA construct according to claim 15.
23. The isolated double-stranded DNA construct according to claim 5, wherein the nucleic acid stuffer fragment is a sequence of 10-50 nucleotides.
24. The method according to claim 7, wherein the nucleic acid stuffer fragment is a sequence of 10-50 nucleotides.
25. The isolated double-stranded DNA construct according to claim 5, wherein the nucleic acid stuffer fragment is a sequence of 50-100 nucleotides.
26. The method according to claim 7, wherein the nucleic acid stuffer fragment is a sequence of 50-100 nucleotides.
27. The isolated double-stranded DNA construct according to claim 5, wherein the nucleic acid stuffer fragment is a sequence of 100-500 nucleotides.
28. The method according to claim 7, wherein the nucleic acid stuffer fragment is a sequence of 100-500 nucleotides.
29. An animal cell comprising the double-stranded DNA construct of claim 4.

Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 8 of 13 of Amendment

30. The isolated double-stranded DNA construct according to claim 4, wherein said region of the target gene is 30 nucleotides long.
31. The method according to claim 10, wherein said region of the target gene is 30 nucleotides long.
32. The isolated double-stranded DNA construct according to claim 4, comprising two identical copies of said structural gene sequence.
33. The isolated double-stranded DNA construct according to claim 4, wherein said region of the target gene is more than 30 nucleotides long.
34. The isolated double-stranded DNA construct according to claim 4, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.
35. The method according to claim 10, wherein said double-stranded DNA construct comprises two identical copies of said structural gene sequence.
36. The method according to claim 10, wherein said region of the target gene is more than 30 nucleotides long.
37. The method according to claim 10, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.
38. An animal cell comprising the double-stranded DNA construct according to claim 30.



Patent Owners : Michael Wayne Graham and Robert Norman Rice  
**Reexamination**  
Control Nos. : 90/007,247 and 90/008,096  
Patent No. : 6,573,099 B2  
Page 9 of 13 of Amendment

39. An animal cell comprising the double-stranded DNA  
construct according to claim 32.

40. An animal cell comprising the double-stranded DNA  
construct according to claim 33.

41. An animal cell comprising the double-stranded DNA  
construct according to claim 34.